CLAIMS

What is claimed is:

1. A nucleic acid mimic in admixture with at least one target molecule selected from the group consisting of nucleic acids, transcription factors, carbohydrates and proteins, said mimic comprising a non-naturally occurring backbone structure to which are appended a plurality of heterocyclic bases,

at least one of said bases being substituted with at least one sterically bulky substituent at a position one, two or three atoms removed from the position of attachment of said base to the backbone.

2. The nucleic acid mimic according to claim 1 wherein said sterically bulky substituent is -R', -OR', -SR', $-N(R')_2$, $-C(R')_3$, $-C(=X)(R')$, $-C(=X)(-Y-R')$ or $S(=O)_{1-2}(-Y-R')$ wherein:

X is O, S or NH;

Y is O, S or NH, and

R' comprises at least 3 atoms and is H, C_1-C_{50}-alkyl, C_2-C_{50}-alkenyl, C_2-C_{50}-alkynyl, C_7-C_{50}-alkyl-aryl, C_6-C_{50}-aryl, C_{10}-C_{50}-naphthyl, C_{12}-C_{50}-biphenyl, C_7-C_{50}-aryl-alkyl, pyridyl, imidazolyl, pyrimidinyl, pyridazinyl, quinolyl, acridinyl, pyrrolyl, furanyl, thienyl, isoxazolyl, oxazolyl, thiazolyl and biotinyl, wherein R' can be substituted one or more times by -NO, $-NO_2$, $-SO_3^-$, -CN, -OH, $-NH_2$, -SH, $-PO_3^{2-}$, -COOH, -F, -Cl, -Br and -I.

3. The nucleic acid mimic according to claim 1 wherein said base is a naturally or non-naturally occurring pyrimidine base.

4. The nucleic acid mimic according to claim 3 wherein said sterically bulky substituent is bound to C-6, C-5 or N-4 of said naturally occurring pyrimidine base.

Christensen et al.
09/142326
fd 1-27-99

530/300

5. The nucleic acid mimic according to claim 4 wherein said sterically bulky substituent is bound to N-4 of said naturally occurring pyrimidine base.

6. The nucleic acid mimic according to claim 5 wherein said naturally occurring pyrimidine base is cytosine.

7. The nucleic acid mimic according to claim 5 wherein said sterically bulky substituent is (C=O)-R'' wherein R'' is C_1-C_{20}-alkyl or C_6-C_{18}-aryl.

8. The nucleic acid mimic according to claim 7 wherein said sterically bulky substituent is (C=O)-C_6H_5.

9. A method for the determination of a nucleic acid comprising:

providing a nucleic acid mimic;

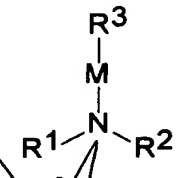
incubating said nucleic acid mimic and said nucleic acid under conditions suitable for the formation of a duplex between said nucleic acid mimic and said nucleic acid; and

determining the occurrence of said duplex as a measure of the occurrence of said nucleic acid;

said nucleic acid mimic comprising a non-naturally occurring backbone structure to which are appended a plurality of heterocyclic bases,

at least one of said bases being substituted with at least one sterically bulky substituent at a position one, two or three atoms removed from the position of attachment of said base to the backbone.

10. A compound for the preparation of a nucleic acid mimic having the general formula:



wherein:

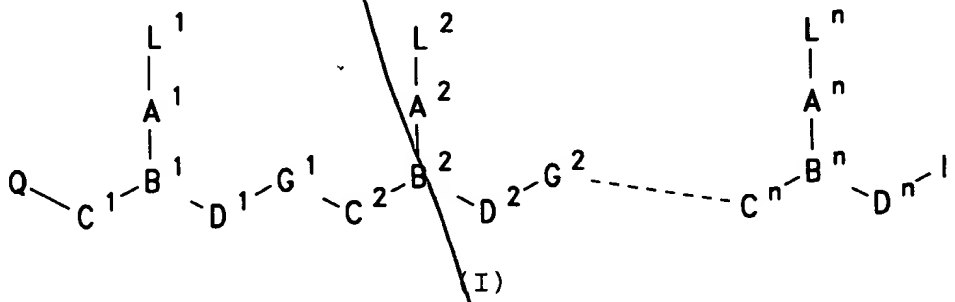
R^1 is C_1-C_4-alkyl having at least one $-COOP^1$, $-NHP^1$, $-OP^1$ or $-SP^1$ group; P^1 is hydrogen or a protecting group;

R^2 is C_1-C_4 alkyl substituted by $-COOP^2$, $-NHP^2$, $-OP^2$ or $-SP^2$, wherein P^2 is hydrogen or a protecting group;

M is a naturally or non-naturally occurring heterocyclic moiety bound to N by a one to three carbon linker; and

R^3 is a sterically bulky substituent containing 3 or more non-hydrogen atoms.

11. The nucleic acid mimic according to claim 1 having formula (I):



(I)

wherein:

n is at least 2,

each of L^1-L^n is independently selected from the group consisting of hydrogen, hydroxy, $(C_1$-$C_4)$alkanoyl, naturally occurring nucleobases, non-naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, heterocyclic moieties, and reporter ligands, at least one of L^1-L^n being said base substituted with at least one sterically bulky substituent;

each of C^1-C^n is $(CR^6R^7)_y$ where R^6 is hydrogen and R^7 is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or R^6 and R^7 are

independently selected from the group consisting of hydrogen, (C_2-C_6)alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6)alkoxy, (C_1-C_6)alkylthio, NR^3R^4 and SR^5, where R^3 and R^4 are as defined above, and R^5 is hydrogen, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6)alkyl, or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

each of D^1-D^n is $(CR^6R^7)_z$ where R^6 and R^7 are as defined above;

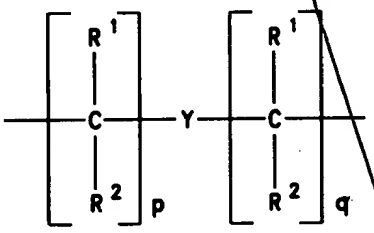
each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

each of G^1-G^{n-1} is $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$ or $-NR^3SO_2-$, in either orientation, where R^3 is as defined above;

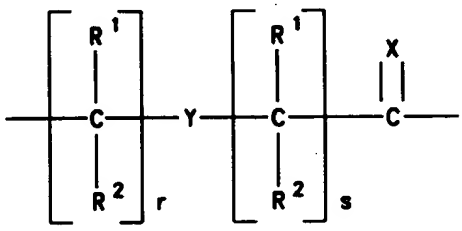
each pair of A^1-A^n and B^1-B^n are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+; or

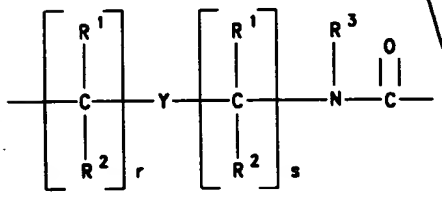
(b) A is a group of formula (IId) and B is CH;



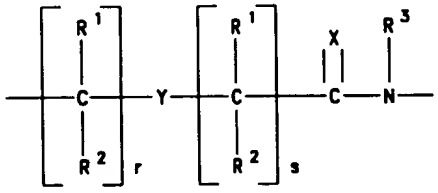
(IIa)



(IIb)



(IIc)



(IId)

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

each R^1 and R^2 is independently selected from the group consisting of hydrogen, (C_1-C_4)alkyl which may be

hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen;

each of G^1-G^{n-1} is $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$ or $-NR^3SO_2-$, in either orientation, where R^3 is as defined above;

Q is $-CO_2H$, $-CONR'R''$, $-SO_3H$ or $-SO_2NR'R''$ or an activated derivative of $-CO_2H$ or $-SO_3H$; and

I is $-NHR'''R''''$ or $-NR'''C(O)R''''$, where R', R", R''' and R'''' are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligonucleotides and soluble and non-soluble polymers.

12. The nucleic acid mimic according to claim 22 wherein said target molecule is a nucleic acid.

13. The nucleic acid mimic according to claim 22 wherein said sterically bulky substituent is -R', -OR', -SR', $-N(R')_2$, $-C(R')_3$, $-C(=X)(R')$, $-C(=X)(-Y-R')$ or $S(=O)_{1-2}(-Y-R')$ wherein:

X is O, S or NH;

Y is O, S or NH; and

R' comprises at least 3 atoms and is H, C_1-C_{50}-alkyl, C_2-C_{50}-alkenyl, C_2-C_{50}-alkynyl, C_7-C_{50}-alkyl-aryl, C_6-C_{50}-aryl, C_{10}-C_{50}-naphthyl, C_{12}-C_{50}-biphenyl, C_7-C_{50}-aryl-alkyl, pyridyl, imidazolyl, pyrimidinyl, pyridazinyl, quinolyl, acridinyl, pyrrolyl, furanyl, thienyl, isoxazolyl, oxazolyl, thiazolyl and biotinyl, wherein R' can be substituted one or more times by -NO, $-NO_2$, $-SO_3^-$, -CN, -OH, $-NH_2$, -SH, $-PO_3^{2-}$, -COOH, -F, -Cl, -Br and -I.

14. The nucleic acid mimic according to claim 22 wherein said base is a naturally or non-naturally occurring pyrimidine base.

15. The nucleic acid mimic according to claim 14 wherein said sterically bulky substituent is bound to C-6, C-5 or N-4 of said naturally occurring pyrimidine base.

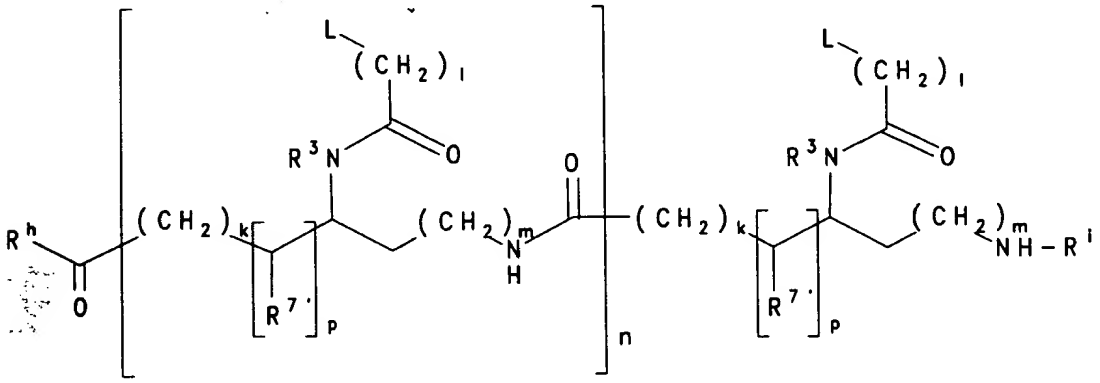
16. The nucleic acid mimic according to claim 15 wherein said sterically bulky substituent is bound to N-4 of said naturally occurring pyrimidine base.

17. The nucleic acid mimic according to claim 16 wherein said naturally occurring pyrimidine base is cytosine.

18. The nucleic acid mimic according to claim 16 wherein said sterically bulky substituent is (C=O)-R'' wherein R'' is C_1-C_{20}-alkyl or C_6-C_{18}-aryl.

19. The nucleic acid mimic according to claim 18 wherein said sterically bulky substituent is (C=O)-C_6H_5.

20. The nucleic acid mimic according to claim 22 having formula (IIIa):



(IIIa)

wherein:

each L is independently selected from the group consisting of hydrogen, phenyl, heterocyclic base moieties, including those substituted with a sterically bulky group or groups, naturally occurring nucleobases, and non-naturally occurring nucleobases, at least one L being said base substituted with at least one sterically bulky substituent;

each $R^{7'}$ is independently selected from the group consisting of hydrogen and the side chains of naturally occurring alpha amino acids;

n is an integer from 1 to 60;

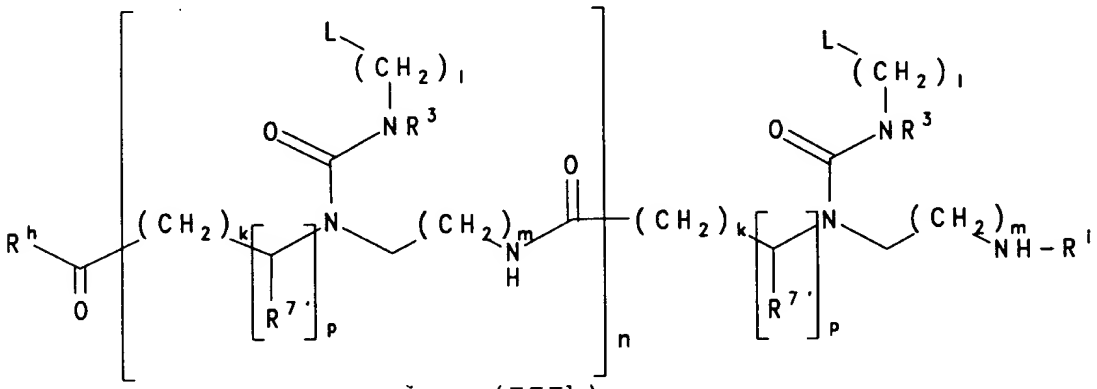
each of k, l, and m is independently zero or an integer from 1 to 5;

p is zero or 1;

R^h is OH, NH_2 or -NHLysNH$_2$; and

R^i is H or $COCH_3$.

21. The nucleic acid mimic according to claim 22 having formula (IIIb):



(IIIb)

wherein:

each L is independently selected from the group consisting of hydrogen, phenyl, heterocyclic base moieties, including those substituted with a sterically bulky group or groups, naturally occurring nucleobases, and non-naturally occurring nucleobases, at least one L being said base substituted with at least one sterically bulky substituent;

each $R^{7'}$ is independently selected from the group consisting of hydrogen and the side chains of naturally occurring alpha amino acids;

n is an integer from 1 to 60;

each of k, l, and m is independently zero or an integer from 1 to 5;

p is zero or 1;

R^h is OH, NH_2 or -NHLysNH$_2$; and

R^i is H or $COCH_3$.